

Applicant : Yurino, et al.
Serial No. : 09/459,712
Filed : December 13, 1999
Page : 4

Attorney's Docket 13452-004001 / PH-710US

REMARKS

Status of the Claims

Pending claims

Claims 7 to 24 are currently pending. Claim 7 has been withdrawn from consideration, thus, claims 8 to 24 are pending and under examination.

Claims canceled and amended

In the present Response, claims 7 and 21 are canceled, without prejudice; and claims 8, 9, 16, and 24 are amended. Thus, after entry of these amendments, claims 8-20 and 22-24 are presented for reconsideration.

Applicants respectfully request entry of the amendments set forth in this response under 37 CFR §1.116. The amendment places the case in condition for allowance and places the case in better condition for appeal; the amendment does not raise any issues of new matter; and, the amended and new claims do not present new issues requiring further consideration or search.

Outstanding Rejections

Claims 8 to 24 stand rejected under 35 U.S.C. §112, first and second paragraphs. The rejection under 35 U.S.C. §102(e) that claims 8 to 21, 23 and 24 are allegedly anticipated by U.S. Patent No. 6,023,540 to Walt et al. (hereinafter "Walt") has been maintained.

Applicants respectfully traverse all outstanding objections to the specification and rejections of the claims.

Drawings

Originally filed sheet of Figures 1, 2C, 3, 7, and 9; and the sheet of Figure 8C submitted August 6, 2001 are replaced under separate cover with newly submitted sheets to correct the drawings as objected to in PTO Form 948. No new matter will be introduced by the amended drawings.

Issues under 35 U.S.C. §112, first paragraph

Claims 8 to 24 are rejected under 35 U.S.C. §112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

No new matter has been added

The Patent Office alleges that new matter has been introduced into the claims via the newly added claims 8 to 24 regarding the immobilization of probes onto the substrate. Two alternative interpretation of claim 8 have been presented; one version explained on page 3, lines 1 to 8, and, a second version, page 3, lines 8 to 10, of the office action. Thus, the Patent Office believes that the claims as pending are unclear.

The claimed invention is directed to methods for detecting the degree of hybridization between a probe and a sample nucleic acid as described by the "second version, on page 3, lines 8 to 10, of the office action. Each probe type is separately immobilized on each different and separate position, or spot, on the array.

Claims 8, 9, and 24 have been amended, and thus dependent claims 10-23, to recite that in part (a) of these claims that each probe type is separately immobilized on each different and separate position.

Applicants believe that the instant amendment addresses the Patent Office's concerns. By the present amendment, no new matter is introduced as support can be found, *inter alia*, on page 5, lines 24-32 of the instant specification. Moreover, it is an inherent property of the claimed invention that the method includes providing a substrate on which each probe type is separately immobilized on a different and separate position, such as found on DNA arrays. Accordingly, Applicants submit that the rejection of claims 8-20 and 22-24 under section 112, 1st paragraph, can be properly withdrawn.

Issues under 35 U.S.C. §112, second paragraph

Claims 8 to 24 are rejected under 35 U.S.C. §112, second paragraph, for allegedly being indefinite.

The phrase "degree hybridization"

The Patent Office alleges that the meaning of the phrase "degree of hybridization" in claims 8, 9, and 24 is unclear. Clarification via clearer claim wording was requested.

Applicants believe the instant amendment addresses the Patent Office's concerns.

The terms "binding" and "hybridization"

The Patent Office alleges that the use of "binding" in claims 16 to 23 causes the claims to be vague and indefinite as to whether some type of binding beyond hybridization is meant.

Applicants believe the instant amendment addresses the Patent Office's concerns.

It is believed that the instant amendment addresses the Patent Office's concerns and the rejection to claims 8-20 and 22-24 under section 112, 2nd paragraph, can be properly withdrawn.

Issues under 35 U.S.C. §102(e)

The rejection under 35 U.S.C. §102(e) that claims 8 to 21, 23 and 24 are allegedly anticipated by U.S. Patent No. 6,023,540 to Walt et al. (hereinafter "Walt") has been maintained. The Patent Office maintains the rejections set forth in the previous office action mailed April 9, 2001 to new claims 8-24.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention

Applicants maintain that Walt does not disclose each and every limitation of the claimed invention and, therefore, does not render the claims unpatentable.

The Patent Office notes that in Walt the quantifying of microspheres with probes on them is deemed a quantifying of probes, albeit not of probe number *per se*.¹

In fact, in the claimed methods the probe number *per se* is detected. This is clarified by the instant amendment; after entry of the amendment the claims will read "detecting the amount of the probe at each position of the substrate." Walt does not disclose detecting the amount of the probe at each position of a substrate.

¹ See the last paragraph, particularly the last three lines, of page 4 of the Office Action.

As noted by the Patent Office, Walt does not measure probe number per se on their microspheres; the quantifying of microspheres with probes on them is not a quantifying of the number of probes. The amount of probes on a microsphere can vary greatly from microsphere to microsphere; thus, it does not follow that quantifying of microspheres is a quantifying of probes. For example, in contrast to the teachings of Applicants' invention, probes 60a, 60b, and 60c of Walt are not labeled with fluorescent marker dyes (Fig. 3 of Walt), and, therefore, cannot be measured by any means taught in Walt.

Moreover, there is no suggestion or motivation in Walt to quantify the amount of probes on a microsphere. In fact, Applicants submit that quantifying the amount of probes on a microsphere was not even contemplated in Walt, as it does not relate to the objectives of Walt. Therefore, while Walt may teach the quantifying of microspheres, it does not teach the quantifying of probes. Applicants have amended independent claims 8, 9, 16, and 24 to recite that the claimed method includes detecting the amount of the probe at each position of the substrate. Support for such amendment can be found, *inter alia*, on page 5, lines 30-32 of the instant specification.

The Patent Office notes that the "argued number of probe molecules is not an instant claim limitation. Rather the instant claims only indicate an 'amount' which lacks any numerical requirement that would distinguish the instant claims from the reference which determines an amount via a normalizing signal."²

Applicants aver that the instant claims do not need to recite a numerical requirement to distinguish them over Walt. In column 15, lines 25-36 of Walt, "normalizing" refers to determining the level of background signal. Applicants do not use "normalizing" to determine the level of background signal. In the instant invention, "normalizing" is used to determine the difference between the amount of the probe biopolymer spotted on the substrate relative to the amount of sample biopolymer. Thus, the claimed invention is distinguishable over Walt without a recitation of a numerical requirement.

In light of the amendment to the claims, and reasons provided, Applicants submit that Walt does not disclose each and every limitation of the claimed invention. Accordingly,

² See page 5, lines 3-8 of the Office Action.

Applicant : Yurino, et al.
Serial No. : 09/459,712
Filed : December 13, 1999
Page : 8

Attorney's Docket No.: 13452-004001 / PH-710US

Applicants aver the rejection to claims 8 to 20, 23, and 24 under section 103, can be properly withdrawn.

CONCLUSION

Claims 8 to 24 are pending in the application. Claim 21 has been canceled; and claims 8, 9, 16, and 24 have been amended by the present Response. Applicants request that the Examiner reconsider the application and claims in light of the foregoing reasons and amendments and respectfully submit that the claims are in condition for allowance.

If, in the Examiner's opinion, a telephonic interview would expedite the favorable prosecution of the present application, the undersigned attorney would welcome the opportunity to discuss any outstanding issues and to work with the Examiner toward placing the application in condition for allowance.

Attached is a marked-up version of the changes being made by the current amendment.

Applicants believe that no fees are necessitated by the present Response. However, in the event any fees are due, the Commissioner is hereby authorized to charge any such fees to Deposit Account No. 06-1050.

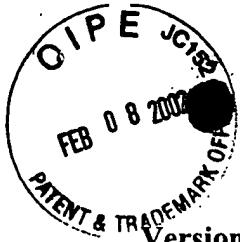
Date:

Jan. 23, 2002

Respectfully submitted,

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Version with markings to show changes made

Applicant : Yurino, et al.

Art Unit : 1631

Serial No. : 09/459,712

Examiner : Arden Marschel, Ph.D.

Filed : December 13, 1999

Title : HYBRIDIZATION DETECTION METHOD AND BIOCHIPS

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FFR 19.2002

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In the claims:

Claims 7 and 21 have been canceled, without prejudice.

Claims 8, 9, 16, and 24 have been amended as follows:

8. (Amended) A method for detecting the degree of hybridization between a probe and a sample nucleic acid, the method comprising

- (a) providing a substrate on which each of a plurality of types of probes is separately immobilized on each different and separate position [are immobilized at a given position];
- (b) providing a sample comprising a nucleic acid;
- (c) contacting the sample with the probe and detecting the amount of the probe at each position of the substrate and the amount of the sample nucleic acid hybridized to the probe, thereby detecting the degree of hybridization between the probe and the sample nucleic acid.

9. (Amended) A method for detecting the degree of hybridization between a nucleic acid probe and a sample nucleic acid, the method comprising

- (a) providing a substrate on which each of a plurality of types of nucleic acid probes is separately immobilized on each different and separate position [are immobilized at a given position];
- (b) providing a sample comprising a nucleic acid;
- (c) contacting the sample with the nucleic acid probe and detecting the amount of the probe at each position of the substrate and the amount of the sample nucleic acid hybridized to the probe; and

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicant: Yurino, et al.
Serial No.: 09/459,712
Filed : December 13, 1999
Page 2 of 3

(d) producing a value representing the degree of hybridization between a nucleic acid probe and a sample nucleic acid by normalizing the difference between the amount of the probe and the amount of the sample nucleic acid hybridized to the probe with the amount of the probe.

16. (Amended) A method for detecting the degree of hybridization [binding] between a probe and a sample comprising a biopolymer, the method comprising

(a) providing a substrate on which each of a plurality of types of probes is separately immobilized on each different and separate position [are immobilized at a given position], wherein the probes are labeled with a first detectable label;

(b) providing a sample comprising a biopolymer, wherein the biopolymer is labeled with a second detectable label;

(c) contacting the sample with the probe and detecting the amount of the probe at each position of the substrate and the amount of the sample biopolymer bound to the probe; and

(d) producing a value representing the degree of hybridization [binding] between a probe and a sample biopolymer by normalizing the difference between the amount of the probe and the amount of the sample biopolymer [bound] hybridized to the probe with the amount of the probe.

24. (Amended) A method for detecting the degree of hybridization between an oligonucleotide probe immobilized onto an array and a sample nucleic acid, the method comprising

(a) providing a substrate on which each of a plurality of types of oligonucleotide probes is separately immobilized on each different and separate position [are immobilized at a given position] to form an array, wherein the oligonucleotide probes are labeled with a first detectable label;

VERSION WITH MARKINGS TO SHOW CHANGES MADE

Applicant: Yurino, et al.

Serial No.: 09/459,712

Filed : December 13, 1999

Page 3 of 3

(b) providing a sample comprising a nucleic acid, wherein the nucleic acids are labeled with a second detectable label;

(c) contacting the sample with the probe and detecting the amount of the probe at each position of the substrate and the amount of the sample nucleic acid hybridized to the probe; and

(d) producing a value representing the degree of hybridization between a probe and a sample by normalizing the difference between the amount of the probe and the amount of the sample nucleic acid hybridized to the probe with the amount of the probe.

In the Drawings:

Originally filed sheet of Figures 1, 2C, 3, 7, and 9; and the sheet of Figure 8C submitted August 6, 2001 are being replaced under separate cover with newly submitted sheets.